3. Understanding the odds-ratio diagrams in the CDSR

Outcomes:

After completing this section you should be confident enough to interpret the analyses for a given review and in particular: -

- *be able to identify the intervention under investigation*
- *be able to identify the outcomes being measured*
- *be able to know whether the results are conclusive or not*
- *to know if the result is good news.*

3.1 Randomised controlled trials and meta analysis

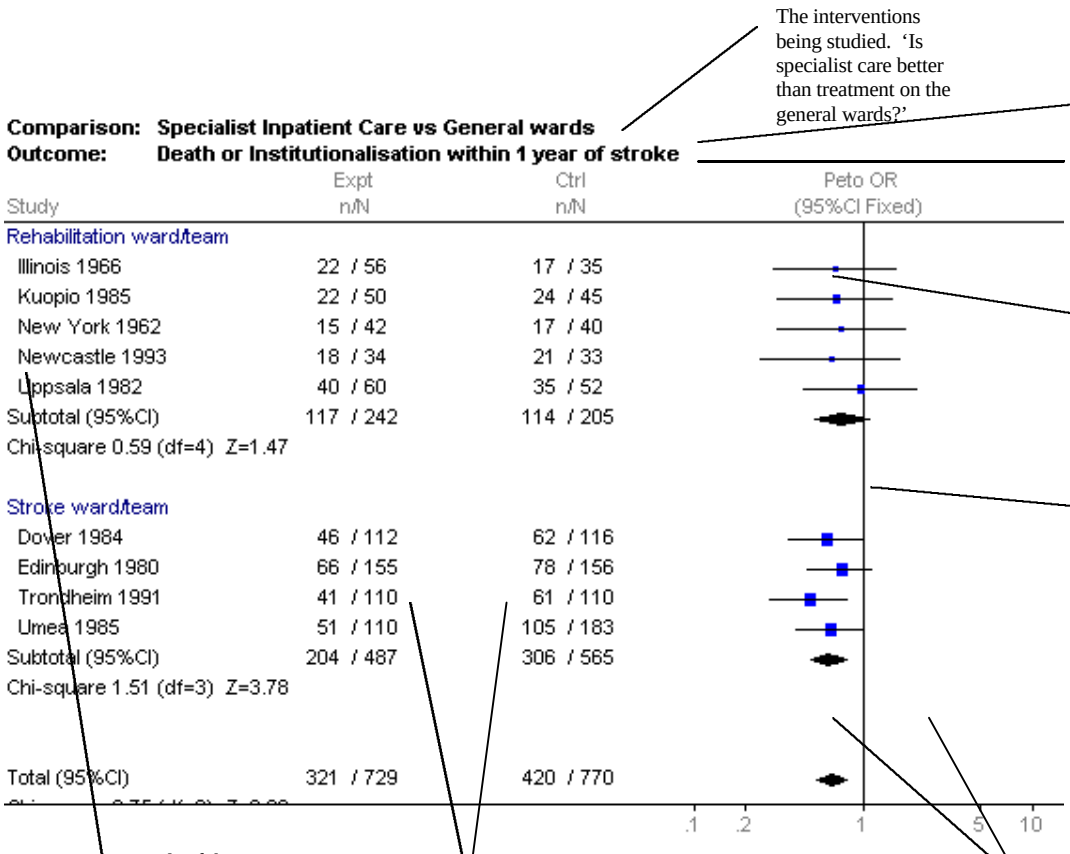
The Cochrane Database of Systematic Reviews on the whole combines the results of individual randomized controlled trials (RCTs). During RCTs, people are randomly divided into two groups: a control group which receives standard (or no) therapy, and a treatment group which receives the treatment under investigation. Specific outcomes are monitored in both groups. Outcomes may be positive, such as remission or cure, or they may be negative, such as relapse or death. At the end of the trial period, the outcomes in both group are compared. The statistical method of combining the results of different RCTs (for the same intervention) is called meta analysis. The results of a meta analysis are presented in the same format as those of a single RCT because they simulate what might have been expected to have occurred had a single trial been conducted equivalent in size to the combination of the individual trials reviewed.

3.2 What is an odds-ratio diagram?

The odds-ratio diagrams presented in CDSR and other good quality systematic reviews are intended to present what are complicated results and concepts in a clear visual fashion. To the uninitiated with little practical knowledge of statistics they appear to be impenetrable at first. However, a little time spent studying them along with a little guidance reveals them to be exactly as intended. The results of long and detailed statistical theory and analysis are made accessible to a wide audience without any real need to understand or explain the background.

Figure 3.1 below shows a simplified odds ratio diagram with all numerical information removed. The diagram shows the odds-ratio diagram for the review of stroke units versus general wards. For each individual trial the odds ratio result is represented by a box. The horizontal line through it represents the confidence interval for that result. The meta analysis result is represented by a diamond, the width of which represents the confidence interval. The horizontal axis shows the odds ratio. The vertical line represents an odds ratio of one and is known as the “line of no effect”.

Figure 3.1 Odds ratio diagram



In order to extract useful information from an odds ratio diagram it is necessary to establish the following:

- The nature of the intervention under investigation which is given in the title of the figure
- The outcomes being measured which are given after the title of the figure
- Whether each outcome is good/positive (of benefit) or bad/negative (of harm)
- Whether the odds ratio for the summary result(s) are greater or less than one (to the right or to the left of the vertical line which represents no effect)
- Whether the confidence intervals (represented by horizontal lines) cross the vertical (no effect) line
- Whether the summary result (at the bottom of the diagram and represented by a black diamond rather than a blue box) 'looks' as if it is a fair representation of the individual trial results

If a bad/negative outcome such as death is measured for a given intervention then a beneficial result will be one in which the odds-ratio is less than one or to the left of the vertical (no effect) line, i.e. the intervention results in less of the outcome and the odds-ratio approximates to the proportion of the treatment group that experience the outcome compared with the control group. Similarly beneficial results for good/positive outcomes have odds ratios greater than one.

If the confidence interval (horizontal) line crosses the vertical (no effect) line then the result (shown by the black diamond for a meta analysis or a blue box for an RCT) does not show a clear or conclusive effect. Confidence intervals used in Cochrane reviews are quoted as either 95% or 99% and the odds-ratio diagrams can be adjusted to show either. In all the following diagrams we have used 95% confidence intervals. The confidence interval represents the range in which we are 95% confident that the 'real' result of the study lies when the result from the individual trial or meta-analysis is extrapolated to the whole of the population which was sampled in the study. Or in other words it means that in theory in 95 out of 100 trials we can be confident that the result will lie somewhere along the horizontal confidence interval lines. If the confidence interval crosses the vertical line then, because we can only be 95% certain that the result is somewhere along that line, it is possible that a result which looks beneficial may in fact be harmful or vice versa. In this situation, the result would be recorded as inconclusive or of uncertain benefit.

The result that you read from the odds-ratio diagram should agree with the textual results and **implications** given in the main body of the review. The visual appreciation of the results of a review would be the first step only in using the results of any review to guide a health care decision.

In summary:

- An odds ratio to the *left* of the vertical line means *less* of the outcome and to the *right more*.
- A *beneficial* result for a *bad/negative* outcome is an odds-ratio of to the *left* of the vertical line (odds ratio of less than one).
- A *beneficial* result for a *good/positive* outcome is an odds-ratio to the *right* of the vertical line (odds ratio of more than one).

Weighted Means Difference (WMD)

Some meta-analysis diagrams include weighted means difference results, which is just a different statistical technique used to deal with different types of outcome. Outcomes can either be dichotomous, yes/no outcomes e.g. death/survival, occurrence of disease/no occurrence of disease. There is no inbetween with dichotomous outcomes, they either happen or they don't. These outcomes can be compared using an odds-ratio. Other outcomes are continuous, they are measured on a continuous scale, e.g. blood loss, length of hospital stay, height, etc. Continuous outcomes cannot be compared using odds-ratio as a statistical method. Instead weighted means difference is used. With WMD the line of no effect falls at 0 instead of at 1 as with odds-ratios, and in the Cochrane Library, WMD results are illustrated using green squares. However, interpretation of the results is exactly the same as with odds-ratio results, e.g. a result lying to the left of the line of no effect (i.e. a WMD of less than 0) means that the outcome under investigation is less likely to occur in the treatment group than in the control group.

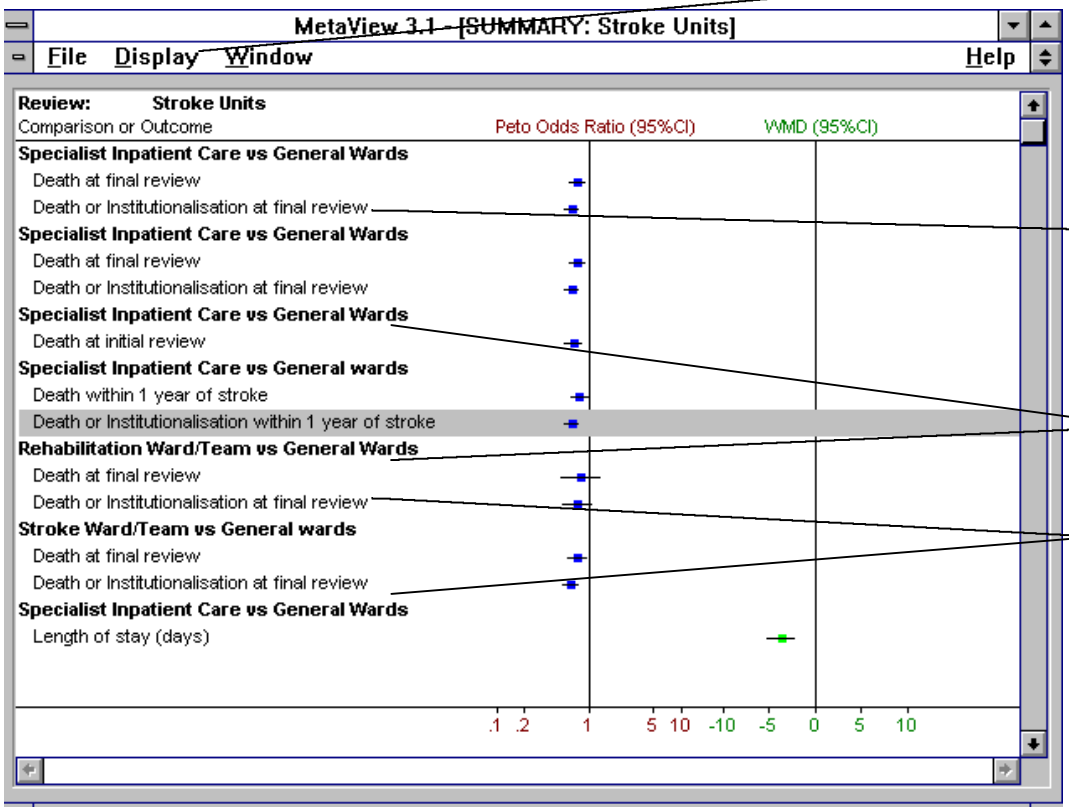
3.3 Worked example

The following example will help to make sense of the information presented in an odds-ratio diagram.

From the main screen of the Cochrane Library locate the review entitled “Stroke Units” by searching for “stroke units”. This review investigates how stroke patients fare when cared for in a specialist inpatient care facility (or “stroke unit” fulfilling the definition of “a multidisciplinary team with a special interest in stroke”) compared with those cared for in a general medical ward.

Select the review (click the mouse on the title) and go to the summary of analyses section. This screen shows the odds ratios for a number of meta analyses for different combinations of comparisons and outcomes, all within the Stroke Units systematic review. **Figure 3.2** illustrates the screen in CLib and shows some of its features.

Figure 3.2 Summary of analysis diagram



The horizontal scale for the odds-ratio can be increased/ decreased from the display menu.

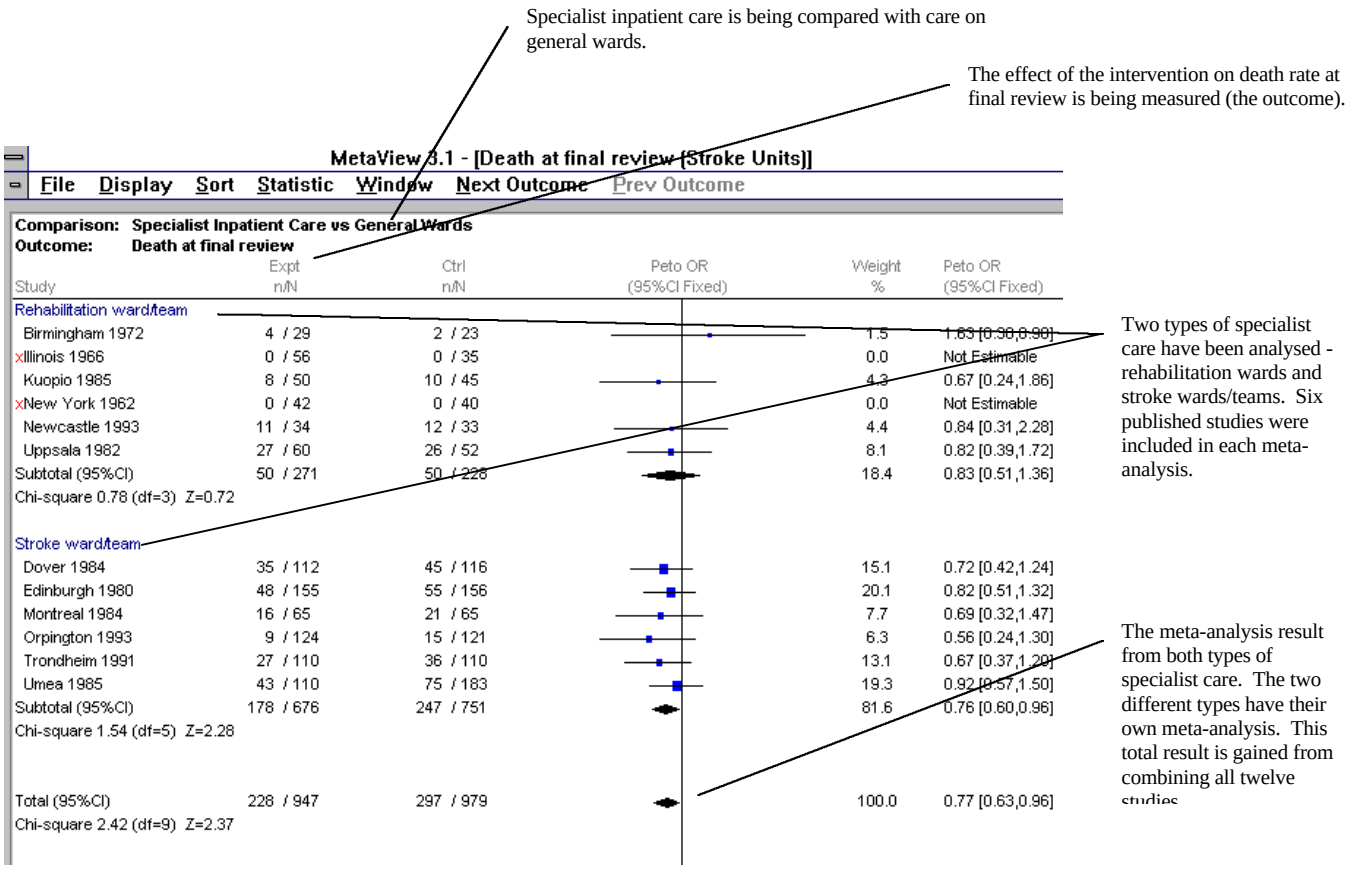
To view the details of the individual studies included in a meta-analysis, double click on the comparison or outcome of interest.

Comparisons are shown in bold in the Cochrane Library.

Outcomes are in normal type.

Double click the mouse on the first comparison, the bold capital heading **SPECIALIST INPATIENT CARE VS GENERAL WARDS,** to reveal the full details of the trials included in this meta-analysis, as shown in **Figure 3.3**. The title of the figure defines the comparison or intervention under investigation which in this case is specialist inpatient care versus general wards. In other words this is a comparison of the care provided to stroke patients in specialist inpatient facilities with that in general medical wards. The outcome listed below is death at final review. This means that the systematic review or meta analysis is comparing the number of people with a stroke who died when cared for in a specialist inpatient facility with those who died in a general medical ward.

Figure 3.3 Full odds-ratio diagram

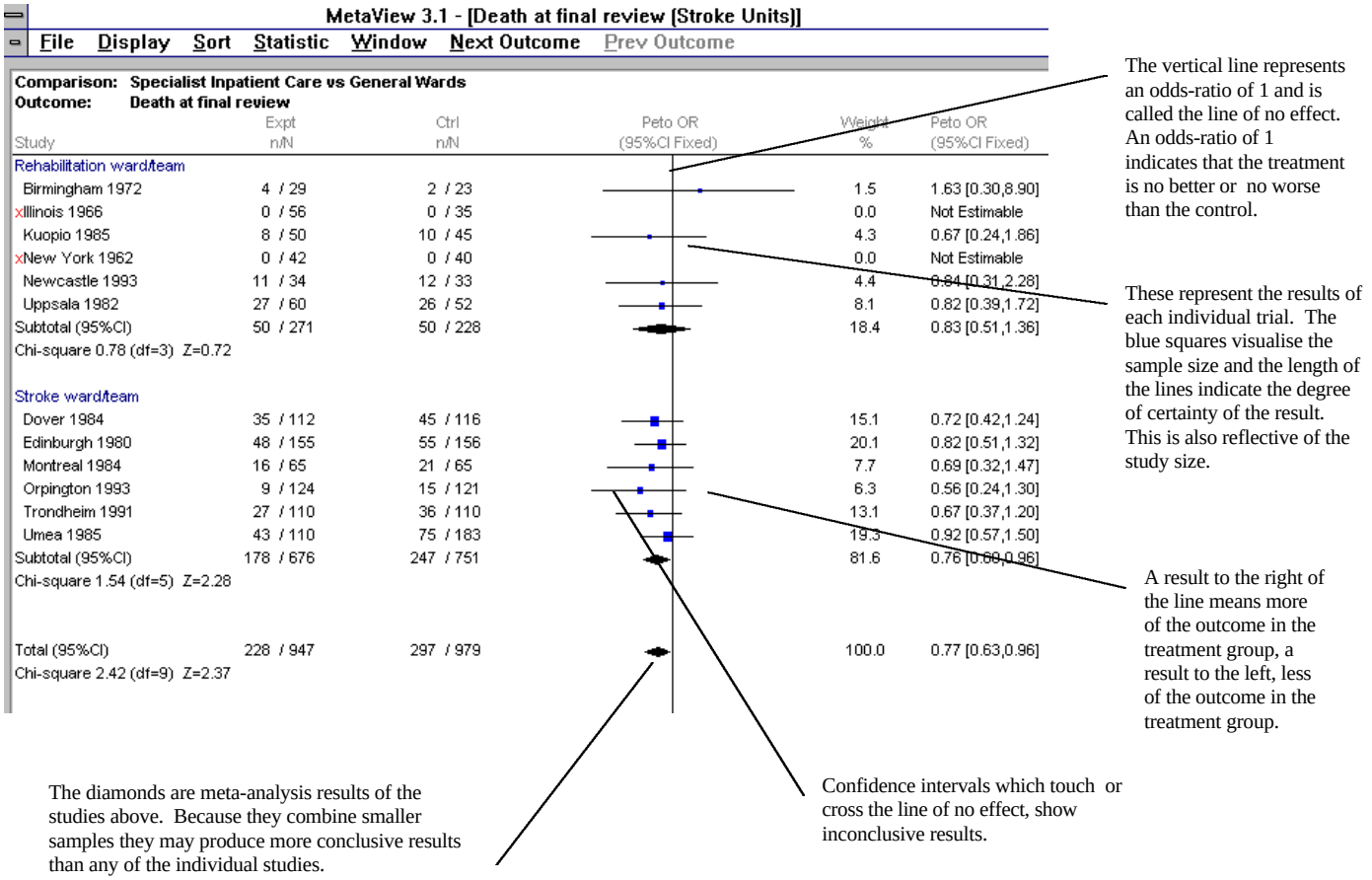


Similar trials within the above review have been grouped together according to particular characteristics, in this case the type of specialist inpatient care (setting) provided, in order to perform several different meta analyses. The first type of specialist inpatient care is a rehabilitation ward or team which is in the top of the diagram and the second is a stroke ward or team which is in the bottom half of the diagram. There were 6 trials which looked at a rehabilitation ward or team as the specialist inpatient care and a further 6 trials which looked at a stroke ward or team as the specialist inpatient care. The trial identifier and some figures for each trial are listed under those sub headings. The odds-ratio result for each trial is shown by a blue box and for each meta analysis by a black diamond. The bottom diamond, shows the result for the total meta analysis for all 12 trials that measured this outcome and comparison.

Some further characteristics of this odds-ratio diagram are shown in **Figure 3.4** below. Looking at the first trial labelled "Birmingham 1972" note that the odds-ratio is greater than 1 (blue box to the right of the line of no effect). This means that stroke patients in the treatment arm of the trial (specialist inpatient care setting) are more likely to die than those in the control arm (general ward). This is because an odds ratio greater than 1 (to the right of the line of no effect) means that the outcome under investigation is more likely to occur in the treatment group than in the control group. In the case of a bad/negative outcome such as death this result means that this trial is showing a harmful effect.

The above does not indicate how certain we are of the result of the trial. This is indicated by the horizontal line through the blue box for the individual trial under investigation. The horizontal line represents the confidence interval for the result derived from the trial. The confidence interval is the range in which we are confident that the "real" result lies when the result of the trial is extrapolated to the whole of the population which was sampled. The diagram illustrates 95% confidence intervals which means that the horizontal line encompasses the range of results in which we are 95% confident that the real result lies. Or in other words in theory we would expect the results of 95 out of 100 trials to lie somewhere along this line.

Figure 3.4 Odds-ratio diagram



The vertical solid black line represents an odds ratio of 1. An odds-ratio of 1 means that the people in the treatment group would have been just as likely to experience the stated outcome as those in the control group and so the treatment has no effect. If a confidence interval crosses the line of no effect then we cannot be sure that the real result of the trial when extrapolated to the population sampled for the study lies the same side of the line of no effect as the trial result. In this situation we would describe the result as of uncertain benefit since the real result could be positive or could be negative. (Note that in the Birmingham 1972 study the blue box is very small and the horizontal line is very large. This is a visual representation of a trial that is very small and therefore has a result with a relatively high degree of uncertainty; the treatment group was only 29 patients and the control group only 23. These numbers are far too small to expect a conclusive or clear result for the size of effect being measured, hence a large confidence interval

Each of the trials in this meta analysis is illustrated below the Birmingham 1972 trial and a blue box or diamond is shown for each result. Below the blue boxes (under the rehabilitation ward stroke team sub heading) is a large diamond which is a representation of the odds ratio and confidence interval for the meta analysis of the 6 trials above it. That is the patients involved in the 6 trials were combined to give a treatment arm of 271 patients in which 50 died and a control arm of 228 patients in which 50 also died. This combined result gave an odds ratio of 0.81 with 95% confidence intervals from 0.49 to 1.33. The results are given in figures further along to the right of the display. The tables show the odds-ratio and confidence interval figures. The odds-ratio implies that the result is beneficial, i.e. less patients dying in the treatment group (about

0.81 times as many or about a 19% reduction) compared with the control group, but the result is uncertain because the confidence intervals cross the line of no effect.

In the bottom half of the screen is a similar meta analysis for trials where the specialist inpatient care was in the form of a stroke ward or team and as for the rehabilitation ward or team each of the individual trials is shown and its odds ratio represented by a blue box and the meta analysis result for those individual trials shown by the second black diamond in the diagram. In the Metaview screen there is a third diamond, which is "off-screen" in **Figure 3.3**, which is the odds ratio for the meta analysis of all of the trials above (the 6 trials where the specialist inpatient care was the rehabilitation ward or team plus the 6 trials where the stroke ward or team was the specialist inpatient care setting). This provided a combined treatment arm of 947 patients in which 228 died and a combined control arm of 979 patients in which 297 died. The odds ratio overall for the combined result is 0.77 with 95% confidence intervals ranging from 0.62 to 0.95.

Overall this meta analysis shows that specialist inpatient care for stroke patients results in less deaths at final review than general wards (about 0.77 times as many or about a 23% reduction) and the result, *with 95% confidence intervals*, is conclusive because the confidence intervals do not cross the line of no effect.

To help you interpret an odds-ratio diagram for yourself, we have provided three self assessment questions and a question grid for you to complete. The grid below shows a review looking at the use of antibiotics to treat sore throats, together with specimen answers.

Title of the review: Antibiotics for sore throat. *Short title as seen in the lists of reviews on the CDSR main screen. Remember to quote the review in full in citations*:-

Del Mar, C.B. Glasziou, P.P. Antibiotics for the symptoms and complications of sore throat (Cochrane Review). In: The Cochrane Library, Issue 4, 1998. Oxford: Update Software.

1. What is / are the intervention(s) under investigation (up to 2)?	**2. What outcome(s) is / are being measured (up to 6) for each intervention?**	**Is effect of intervention conclusive?**	**Is intervention beneficial, harmful or uncertain?**
a. *Antibiotics vs. control for the treatment of sore throat*	**a.** *Incidence of acute rheumatic fever within 2 months*	Yes	Beneficial
	b. *Incidence of otitis media within 14 days*	Yes	Beneficial
	c. *Incidence of sinusitis within 14 days*	No	Uncertain
	d. *Incidence of quinsy within 2 months*	Yes	Beneficial
	e. *Incidence of acute glomerulonephritis within 1 month*	No	Uncertain
b. *Antibiotics vs. control for the treatment of sore throat*	**a.** *Symptom of sore throat on day 3*	Yes	Beneficial
	b. *Symptom of sore throat on day 3: blind vs. unblinded studies*	Yes	Beneficial
	c. *Symptom of sore throat on day 3: antipyretics vs. no antipyretics*	Yes	Beneficial

3.4 Self assessment exercises

Now try to answer the questions for the following reviews by completing the tables below. Aim to spend no more than ten minutes on each review, simple answers are all that is needed. If unsure about any of the results you can cross check your decisions with those in the implications or results sections of the review. You will find that it takes longer to look up and read even the simple bottom line result from the text. Answers are given at the end of the section.

Reviews:

1.Vandekerckhove P, Watson A, Lilford R, Harada T, Hughes E. Therapeutic effect of oil-soluble and water-soluble media used for tubal patency testing (hysterosalpingography or laparoscopy) on pregnancy rates in infertility patients (Cochrane Review). In: The Cochrane Library, Issue 4, 1998.
Oxford: Update Software.

2. Enkin MW, Wilkinson C. Manual removal of placenta at Caesarean section (Cochrane Review). In: The Cochrane Library, Issue 4, 1998. Oxford: Update Software.

3. Counsell C, Sandercock P. Anticoagulant therapy compared to control in patients with acute presumed ischaemic stroke (Cochrane Review). In: The Cochrane Library, Issue 4, 1998. Oxford: Update Software.

Title of the review: Flushing of the fallopian tubes in infertility

1. What is / are the intervention(s) under investigation (up to 2)?	2. What outcome(s) is / are being measured (up to 6) for each intervention?	Is effect of intervention conclusive?	Is intervention beneficial, harmful or uncertain?
a.	**a.**		
	b.		
	c.		
	d.		
	e.		
	f.		
	g.		
	h.		
	i.		
	j..		
b.	**a.**		

Title of the review: Manual removal of placenta at CS

1. What is / are the intervention(s) under investigation (up to 2)?	2. What outcome(s) is / are being measured (up to 6) for each intervention?	Is effect of intervention conclusive?	Is intervention beneficial, harmful or uncertain?
a.	**a.**		
	b.		
	c.		
	d.		
	e.		

Title of the review: Anticoagulants in acute stroke

1. What is / are the intervention(s) under investigation (up to 2)?	2. What outcome(s) is / are being measured (up to 6) for each intervention?	Is effect of intervention conclusive?	Is intervention beneficial, harmful or uncertain?
a.	**a.**		
	b.		
	c.		
	d.		
	e.		
	f.		
	g.		
	h.		
	i.		
	j.		
	k.		
	l.		

Answers to Self Assessment Questions in section 2.4 questions (correct for Issue 4, 1998)

1. Search for "Canada" and look in the Cochrane Centres database. The contact is given as Kathie Clark and the e-mail address given in the contact section is E-mail: cochrane@fhs.mcmaster.ca

2. Click on the **Cochrane Collaboration Handbook** on the button bar. Section 5 covers "Locating and selecting" studies, and if you scroll down you will see section 5.4 deals with electronic databases - including trials registers, which can be found listed in Appendix 5a.

3. There is a possible Methods Working Group listed for health economics. This can be found simply by browsing down the index window - under the Cochrane Collaboration heading. The contact is Dr. Miranda Mugford, at University of East Anglia. A search on "economics" found several hits in the method groups, fields groups and networks database. Note, because the search covers all text not all will be relevant; one of these is someone from the nursing network who is based at the Centre for Health Economics.

4. Sources of support are listed in the details for the Review Groups: Janssen-Cilag Ltd UK, Eli Lilly Pharmaceuticals UK, NHS Executive, Anglia and Oxford Research and Development Programme UK, NHS Executive Research and Development UK, Mental Health Branch, Queensland Health Australia, Helsinki University Central Hospital Finland

5. Look in the Review Groups database and double click on the cystic fibrosis group . Use the Search dialog to find "statistical" and you will see that it is Prof. Deborah Ashby (UK)

6. References cited in the review text are usually listed in the **References** section. Look for the corticosteriods review and then use the right click mouse button to go to references section. Each RCT may have several citations.

7. The International Register of Vision Trials (IRVT), plus additions from current searching activity are the basis for the trials register for this group.

8. Look in the Index window under the Collaborative Review Groups entry - there is a listing of reviews and protocols ordered by CRG, in 'Summary of CRG output'.

9. A search for "BREAST SCREEN*" produces 44 hits. It retrieves some hits that don't seem particularly related to the subject, but remember that this is because you are always searching through the full text of the Cochrane Library. We need to combine terms to fully cover the database. Below is a suggested search:-

#1	BREAST*
#2	"BREAST SCREEN*"
#3	"MASS SCREEN*"
#4	MASS SCREENING:ME
#5	MAMMOGRAPHY:ME
#6	MAMMOGRAPHY
#7	#3 OR #4 OR #5 OR #6
#8	#1 AND #7
#9	#2 OR #8

As you can see you find 18 hits in the DARE database. Records in the 'Database of quality assessed reviews' have been subjected to and have met the quality criteria applied by CRD, related to the methodology of the systematic review. Records in the 'Other assessed reviews' section have been assessed, but for whatever reason don't meet the CRD criteria, but are included as potentially useful bibliographic sources for further reviews.

10. You should have found an article in the Review Methodology database by Shapiro - "Meta-analysis/Shmeta-analysis".

11. After doing an author search, you could restrict your search to 1994 to speed up retrieval. "Meta-analysis and its problems".

12. a. Blood loss, post operative morbidity.

b. Two. In Hershey 1978, 386 consecutive caesarean patients section in a county hospital of which 78 (20%) were excluded from the analyses. In McGann 1993, 100 patients. (from "Characteristics of included trials" section)

c. You can find this out from the "cover sheet" section of the review. Since 1998: Issue 2, the citations for references in the CDSR have shortened. For this example:-
Enkin MW, Wilkinson C. Uterine exteriorization vs intraperitoneal repair at Caesarean section (Cochrane Review). In: The Cochrane Library, Issue 3, 1998. Oxford: Update Software.

d. This information can be found in the "Conclusions" section of the review. Each Cochrane Review gives 'Implications for practice' and 'Implications for research'. In this case the advice for practice, is not particularly positive.

Answers for Section 3.4 Self assessment exercises (correct for Issue 4, 1998)

1. Title of the review: Flushing of the fallopian tubes in infertility

1. What is / are the intervention(s) under investigation (up to 2)?	**2. What outcome(s) is / are being measured (up to 6) for each intervention?**	**Is effect of intervention conclusive?**	**Is intervention beneficial, harmful or uncertain?**
a. *Oil soluble contrast media vs. water soluble, for tubal flushing*	**a.** *Pregnancy rate (overall)*	Yes	Beneficial
	b. Pregnancy rates (sub-groups)	Yes	Beneficial
	c. *Image quality of ampulla*	Yes	?
	d. *Image quality of uterine cavity*	Yes	?
	e. *Immediate pain*	No	Uncertain
	f. *Delayed pain*	Yes	Beneficial
	g. *Volume of contrast medium used*	Yes	Beneficial
	h. *Intravasation rate*	Yes	?
	i. *Infection rate*	No	Uncertain
	j. *Incidence of hemorrhage*	Yes	Beneficial
b. *Water soluble contrast media vs no treatment for tubal flushing*	**a.** *Pregnancy rate*	No	Uncertain

2. Title of the review: Manual removal of placenta at CS

1. What is / are the intervention(s) under investigation (up to 2)?	2. What outcome(s) is / are being measured (up to 6) for each intervention?	Is effect of intervention conclusive?	Is intervention beneficial, harmful or uncertain?
a. *Manual removal of placenta vs spontaneous separation at caesarean section*	**a.** *Blood loss*	Yes	Harmful
	b. *Postoperative drop in haematocrit*	Yes	Harmful
	c. *Transplacental bleeding (Kleinhauer)*	No	Uncertain
	d. *Significant (>0.1 ml) transplacental bleed*	No	Uncertain
	e. *Endometritis*	Yes	Harmful

3. Title of the review: Anticoagulants in acute stroke

1. What is / are the intervention(s) under investigation (up to 2)?	**2. What outcome(s) is / are being measured (up to 6) for each intervention?**	**Is effect of intervention conclusive?**	**Is intervention beneficial, harmful or uncertain?**
a. *Anticoagulant vs control in acute presumed ischaemic stroke*	**a.** *Dead or dependant at end of scheduled follow-up*	Yes	Beneficial
	b. *Death from all causes at various times during follow-up **	No	Uncertain *
	c. *Early death from all causes (within 1 month)*	No	Uncertain
	d. *Late death from all causes during follow-up > 1 month*	No	Uncertain
	e. *Death from vascular causes during follow-up > 1 month*	No	Uncertain
	f. *Deep venous thrombosis during treatment period*	Yes	Beneficial
	g. *Pulmonary embolism during treatment period*	no	Uncertain
	h. *Symptomatic intracranial haemorrhage during treatment*	no	Uncertain
	i. *Any intracranial haemorrhage - systematic CT*	no	Uncertain
	j. *Recurrent ischaemic/unknown stroke during treatment*	no	Uncertain
	k. *Any recurrent stroke or systematic intracranial haemorrhage during treat.*	no	Uncertain
	l. *Major extracranial haemorrhage during treatment period*	no	Uncertain

*** The results actually vary depending on the period of follow-up.**